EXHIBIT 1

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whether a study supports an association or not. I'm not looking to go into an interpretation. My question is very simple.

Is there any article you can point to where the authors conclude unequivocally olmesartan is not associated with either olmesartan-associated enteropathy, sprue-like enteropathy, olmesartan-induced enteropathy, however you want to name the condition? Any one where the authors make that conclusion, it did not associate it. Can you point to any article?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: So, again, just because they choose to write something doesn't mean that that's what their article showed. Their article showed that there was no association when the data were considered --

BY MR. SLATER:

Q. Move to strike.

A. -- in an unbiased manner.

Q. Move to strike.

Doctor, it's a really simple question.

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Is there any article you can point to where that is the explicit conclusion in the article?

A. Well, I think Greywoode does come to that conclusion.

Q. Okay. Any others?

Well, rephrase.

So you think Greywoode concludes unequivocally there's no association, even though they say that this sprue-like enteropathy recently associated is a rare event, and even though they say olmesartan causes severe sprue-like enteropathy; right? That's what you're telling the jury and the judge; right?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I'm saying that a key point to interpreting literature is to have access to the data within the paper and to be able to form your own conclusion, and my interpretation of their data is crystal clear. That there was no association in that study.

BY MR. SLATER:

Q. Okay. All right. Move to strike.

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Doctor, let's -- let's try to get on the same page because it's -- I realize what you're trying to do, but it's starting to obstruct my time.

I am not asking you to interpret the data and tell me your opinion about whether the data supports an association or not. So I would appreciate it if you would stop answering the questions as if that's what I'm asking. It's a very simple question.

Is there any article where there's an explicit conclusion by the authors that olmesartan is not associated with sprue-like enteropathy, olmesartan-associated enteropathy, or any other way you would describe that condition? Is there any article that makes that explicit conclusion; yes or no?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: So my concern is that for reasons that are not clear to me that authors that are providing data, as was also seen in the Lagana study that are also completely negative, are feeling

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compelled to keep referring back to these case series. So they're -- they're sort of dampening down the evidence from their own study for reasons that I don't understand.

So I don't think anybody wrote that there was no association because of the Mayo case series. However, the Lagana study is also a negative study.

BY MR. SLATER:

Q. Move to strike.

Is the answer no, there's no such article you can point to?

A. I'm not aware of any article where the only conclusion, the only thing that was stated at the end of the article was that there's no association.

Q. You're not aware of any article that actually reached the conclusion and said explicitly there is no association; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: How about if I read you this sentence from Lagana in the abstract:

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"There were no statistically significant differences between olmesartan users with abdominal pain and controls for any single histopathological abnormality."

BY MR. SLATER:

Q. Okay. Move to strike as nonresponsive.

I'm correct that there's no article where the authors conclude there is no association; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I'm going to look at another one that was negative and see what they wrote.

I guess I will say that no author felt that they could safely state that, even though their data suggested the otherwise.

BY MR. SLATER:

Q. Move to strike after the word "that."

Am I correct that there is no article you can point to where the authors

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conclude explicitly and unequivocally olmesartan does not cause sprue-like enteropathy, olmesartan-associated enteropathy, or any other term you would use to cause that condition? There's no other such article that draws that conclusion; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: Well, I think we have to agree to disagree because I think I've already answered that question.

BY MR. SLATER:

Q. Well, this was a question about causation as opposed to association.

So with regard to the word "causation," there's no article you can point to that reaches that conclusion; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I just cited two articles that I think support that conclusion.

BY MR. SLATER:

Q. Let's look at -- well, rephrase.

One of the articles is Greywoode where they say in the conclusion that olmesartan

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causes severe like sprue-like enteropathy. That's one of the ones you're relying on; right?

MR. CHRISTIAN: Objection. Form.

BY MR. SLATER:

Q. It's a yes or no question. Correct?

MR. CHRISTIAN: Objection. Form.

MR. SLATER: (Laugh).

THE WITNESS: (Reviewing document).

I mean, you're getting really down to technicalities because the conclusion of the Greywoode paper is talking about a recent association, and then they're saying future studies should focus on the mechanisms, but I don't think that that means that they think it causes it.

BY MR. SLATER:

Q. Actually, Doctor, your testimony for this jury is that the Greywoode article concludes there's no causal relationship between olmesartan and sprue-like enteropathy, even though in the conclusion the authors say future

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studies should focus on the mechanisms by which olmesartan causes severe like -- severe sprue-like enteropathy ; correct?

It's a yes or no. That's correct; right? That's what you're telling this jury?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: What is correct?

BY MR. SLATER:

Q. You didn't understand my question?

A. It was too long. Could you just break it down?

Q. Let's break it down? Okay. I'm going to break it down.

You're telling the jury that the Greywoode article concludes that olmesartan does not cause sprue-like enteropathy, even though in the conclusion they say that future studies should focus on the mechanisms by which olmesartan causes severe sprue-like enteropathy; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: So what I said was,

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their data presented in that article do not support an association or a causation. I can't speculate as to what compelled them to write that sentence that refers back to case series.

BY MR. SLATER:

Q. Okay. Move to strike.

The answer is -- well, rephrase.

My question is not predicated on you interpreting the validity of what people said or what you would have said in a conclusion based on the data you read.

You understand that; right? I'm not asking you to interpret the data for this question. Do you understand that?

MR. CHRISTIAN: Objection.

THE WITNESS: I don't agree with your question asking me to do that.

Can't hear you.

BY MR. SLATER:

Q. If we can't get done in seven hours, you've been evading these questions for so long, I'm going to ask for more time. So let's try to stick to my questions instead of you

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telling me you're talking points about not agreeing. We already know what you agree or don't agree with.

So I'm going to try to go through my questions now and ask you to actually try to answer them directly.

MR. CHRISTIAN: Objection, Adam.

BY MR. SLATER:

Q. So I'll ask the question again.

MR. CHRISTIAN: He's been answering the questions appropriately.

MR. SLATER: No, he hasn't, and when you suggest that, it's misleading and it's disingenuous because he hasn't been.

MR. CHRISTIAN: I disagree.

MR. SLATER: My questions are very clear. I keep asking him not to do interpretation, and he keeps doing it. He's wasting my time and he's dragging this deposition out, okay?

MR. CHRISTIAN: Let's just ask your question. Move on.

BY MR. SLATER:

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Q. So here's the question, Doctor. Focus. Here's the question.

MR. CHRISTIAN: Objection.

BY MR. SLATER:

Q. Is there any article where the authors write the words "olmesartan does not cause sprue-like enteropathy, olmesartan enteropathy" or however they might characterize that condition, where there's an explicit conclusion it doesn't cause this condition? Is there any article that says that?

A. Not --

MR. CHRISTIAN: Objection. Form.

THE WITNESS: Not to my knowledge.

BY MR. SLATER:

Q. I want to be very clear for the jury.

Do you think that olmesartan-associated enteropathy, by whatever label you want to put on it, should be evaluated as a drug allergy in determining whether there's causation or not; yes or no?

A. I'd say no. I said no.

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Q. You say that diarrhea -- this is number 3 of your comments on the Rubio-Tapia article -- that diarrhea was noted to have been a symptom for a median of 19.2 months; right?

A. Correct.

Q. Based on that, so this was generally not a syndrome of rapid onset in the majority of patients.

That's what you wrote; right?

A. Yes.

Q. Okay. The duration for which the symptom exists does not tell us whether it was a syndrome of rapid onset; correct?

A. I don't think I understand that question.

Q. There can be a condition where there's a rapid onset where the patient can point to that's when I got sick, that's when the diarrhea got really bad, that's -- that's when I -- when it hit me, and then the condition can last for 19 or 20 months.

So you could have rapid onset, and then it could last for 20 months after that; right?

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A. That was not really what was described in the case series, no.

I was, you know, all of these points I was making, I was trying to highlight, simply highlight the main findings of the paper. So that when I looked at other literature, since this was the original paper, I could find a way to put the other papers in context with this one.

So that's just basically what they said.

Q. Okay. Well, if I want to understand your methodology and reasoning, we can go through this and see what you think; right?

A. Sure.

Q. This teaches us your thinking; right?

A. Okay.

Q. And to the extent that you said things in here that are un -- that are incorrect or unsupportable, that could undercut the opinions you formed in this case; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I don't see how in any way me listing the median number of

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months could be unsupportable. That's -- that's what they wrote in the paper.

BY MR. SLATER:

Q. Well, that's going to be for someone else to decide who's a fact-finder in this case, but the fact is, if you made mistakes or made assumptions that are not factually accurate, that could undercut the opinions that you formed based on those assumptions; right?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: Sure.

BY MR. SLATER:

Q. Well, let's look at this, and I'll ask you this question.

Actually, let me ask you this.

Are you aware of whether most patients who are diagnosed with olmesartan-associated enteropathy can pinpoint the point in time when they felt that they got very sick and they can say yes, this is when I became ill?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: So I -- as I mentioned before, I reviewed two of the

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plaintiff cases, and that's exactly what happened.

BY MR. SLATER:

Q. Okay. And just to be clear, you've reviewed two cases. Those are the only two cases of potential olmesartan-associated enteropathy you've ever reviewed in your life; correct?

A. Well, other than these papers where they are summarizing 22 cases and then other reports where they're summarizing cases. So that's a modest amount of information. It's not the same as reading a four-inch chart, but it's some interest in knowing about the cases.

Q. You'll agree with me then that patients with olmesartan-associated enteropathy where it's diagnosed, most of those patients can actually identify when they had the onset. They can say, this is when the onset of the disease occurred acutely. They can remember what occurred; right?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I can't really say. I can only talk about the two cases where

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there seemed to be a pretty good sense of them.

BY MR. SLATER:

Q. So you don't know the answer to that question?

A. Because I don't have access to all the charts from all of these patients.

Q. The answer is you don't know; right?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: Can you --

BY MR. SLATER:

Q. I'm sorry. I couldn't hear you.

A. Could you restate the question?

Q. You don't have an opinion one way or another as to whether patients can pinpoint when they got sick with this condition in terms of an acute onset. You don't have an opinion one way or the other; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I suppose I don't have a definitive opinion, no, because -- because I haven't seen the individual cases here.

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BY MR. SLATER:
Q. Okay. In your list of observations about this article in number 4, you point out all the patients had weight loss; right?
A. Right.
Q. That's a unifying feature of these patients; correct?
A. In this particular study.
Q. Eight of the patients had their stool tested, and they were found to have steatorrhea; correct?
A. Correct.
Q. That's a sign of malabsorption; correct?
A. Yes.
Q. You don't believe it's a coincidence that all eight patients who are tested actually had steatorrhea. You're not thinking that's a coincidental finding, are you?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: No. I'm trying to lay out that in some of the patients they tested it and some of them had it.

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BY MR. SLATER:
Q. Well, every patient they tested for it had this condition; right?
A. But the most likely thing is, you wouldn't test a patient for it if -- let's say you had diarrhea and I asked you, so does your stool flow? Is your stool foul smelling? Do you see oil droplets in your stool? And you say no, never. Then I might not think to send off a fecal fat, at least in an initial assessment.
Q. Move to strike.
Each of the eight patients who were testified had this finding; correct?
A. Yes.
Q. At least among those eight patients, that's a unifying feature; correct?
A. But that's my exact point. There's -- there's a bunch of other patients in this study that comprise the 22. So we don't know about them. So we don't know if it's a unifying feature.
Q. Doctor, you realize these are patients who were being evaluated by the Mayo Clinic where the Mayo Clinic only figured out

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later what had happened with these patients, and then surmised that it was the olmesartan causing these patients' condition.
They didn't know about the association between olmesartan and this type of a clinical presentation when they were working these patients up. You know that; right?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: Yes.
BY MR. SLATER:
Q. Okay. Number 6, the serological test for celiac disease IgA tissue transglutaminase was negative in all patients in the study; correct?
A. Yes.
Q. That is a unifying feature; correct?
A. Correct.
Q. Did not have celiac disease; correct?
A. I didn't hear that exactly.
Q. Do you agree with me that these 22 patients did not have celiac disease?
A. That's a really interesting point

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that you raise because in the follow-up paper from the same group, they indicated that several of the patients were later discovered to have celiac disease.
Q. Actually, that's the Cartee/Murray paper where they weren't talking about the same patients; right?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: The way that paper is written, which is in a non-PubMed journal, it's really hard to know who they were talking about. I interpreted it as that they were basically talking about the same patients.
BY MR. SLATER:
Q. If they weren't talking about the same patients, your assumption drops out and it undercuts your opinion; correct?
A. Well, if they're considered the experts about what this syndrome is, even if they are other patients, if you now have patients that you say, oh, when we worked them up, we didn't think they had celiac disease but later they did, then it undercuts their insinuation in this first

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paper that, by definition, patients who have this syndrome cannot have celiac disease.

Q. Move to strike.

Let's come back to my original question.

The 22 patients in this study did not have celiac disease more likely than not; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: At the time this paper was submitted.

BY MR. SLATER:

Q. So you agree with me; right?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: As written in 2012, yes.

BY MR. SLATER:

Q. Would you say to a reasonable degree of medical probability, even having read the subsequent paper, that any of these patients had celiac disease? You can't say that; right?

A. I think I can say that it's my interpretation of the follow-up paper that some of them probably did have celiac disease.

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Q. Okay. Which of the patients had celiac disease based on your interpretation of the subsequent paper, which we agree is not talking just about these 22 patients but is talking about other patients?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: So it would have been nice if they had included in Table 1 some sort of deidentified code for each patient, and then it would have been nice in the Martee paper if they had provided actual data rather than just a free-form discussion. There is no actual data presented in the Martee paper -- Cartee paper.

BY MR. SLATER:

Q. Based on the data that you have available, short of speculating, you can't say to a reasonable degree of medical certainty that any of the 22 patients had celiac disease; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I'd like to take a minute to look at the Cartee paper before I answer that.

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I don't have it handy. I think it's in the back here maybe.

(Reviewing document).

So to me the way I read this sentence is it's more likely than not that they are talking about the same patients. It says -- I mean, they keep citing reference 4, which is their Mayo case series.

So they talk about repeat endoscopy and follow-up and that's -- I'm on -- I'm on page 4 of 8 of this article on the right column.

They say "repeat endoscopy biopsy showed histologic improvement," and they refer to reference 4.

Then in the next paragraph:

"Several patients had a prolonged course of symptom resolution or have yet to make a complete clinical recovery. Several received Infliximab and budesonide. After the diagnosis and treatment for OAE, several patients seen at the Mayo Clinic likely had underlying

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clinical disease as evidenced by symptoms with reinstitution of gluten into the diet."

MR. CHRISTIAN: I think you said "clinical." You see that?

THE WITNESS: What's that?

MR. CHRISTIAN: You misread. See that?

THE WITNESS: Oh. "Several patients seen at the Mayo Clinic likely had underlying celiac disease as evidenced by symptoms with reinstitution of gluten into the diet."

So I thought it was implicit that they were talking about the same patients.

BY MR. SLATER:

Q. So you think that the Cartee/Murray article titled "Sprue-Like Enteropathy Associated With Olmesartan" is discussing the same 22 patients as described in the Rubio-Tapia 2012 article?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: It's my --

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BY MR. SLATER:
Q. Do you think it's identical patients, patient group?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: They don't specify. So obviously I can't say if it's exactly the same 22, but I think it's implicit because they just referenced their paper in the preceding sentence that I think they're talking about the same patients.
BY MR. SLATER:
Q. If you're wrong and the Cartee/Murray paper is not limited to the same 22 patients, that undercuts your opinion; correct?
A. Well, let's put it this way. I think it could be that there could be some additional patients, but that doesn't undercut my opinion. Because if it's patient 23 and 24, it just indicates the original case series was too small.
Q. Do you see that they actually cite case reports of patients they didn't even treat in this article and discuss those as well?
A. Yes.

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Q. Did you notice that?
A. Yes.
Q. Okay. It's clearly not an identical group of patients; right?
A. I can't answer that. I don't know.
Q. Discussed patients in this article, the Cartee/Murray article, from case reports that they didn't even treat. So it's not the same 22 patients; right?
A. But when they said "after the diagnosis for OAE, several patients seen at the Mayo Clinic," those other case series they're talking about are from other locations.
Q. They can be talking about other patients seen at the Mayo Clinic not in the original 22; right?
A. Yes.
MR. CHRISTIAN: Objection.
BY MR. SLATER:
Q. You don't know the answer of what they're -- whether they are or they're not; right?
MR. CHRISTIAN: Objection. Form.

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THE WITNESS: That's correct. Can't hear you.
BY MR. SLATER:
Q. On that, you can't say to a reasonable degree of medical certainty that any of the 22 original patients had celiac disease; correct?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: I can't say a hundred percent because of the very limited quality of this evidence in these articles.
BY MR. SLATER:
Q. You talk about the HLA-DQ genetic testing; correct?
A. Yes.
Q. Number 7?
A. Yes.
Q. And you point out that this was positive in 17 out of 21 patients; right?
A. Right.
Q. HLA-DQ typing would be positive in 95 percent or more in celiac patients; right?
A. Right.

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Q. You say this "Strongly suggests that some of these patients may have had a genetic predisposition to an autoimmune pathology"; right?
A. Right.
Q. That would speak to the mechanism and to who's predisposed, but would not disprove causality; correct?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: So what I'm getting at there is this idea that if it was just simple causation, then you give the drug and X percent of people should get the syndrome regardless of any features of those individuals.
You could walk into Norway, Canada, Mexico, United States, African American, Asian, white, doesn't matter. You give the drug, boom, they get the syndrome.
And what I'm trying to say here is, there's some genetic predisposition, but obviously I can't speculate anything more than -- than that.

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BY MR. SLATER:
Q. People who develop celiac disease have a genetic predisposition to celiac disease; right?
A. So I think that that's still being worked out. Because a positive HLA-DQ2 and DQ8 does not mean that they have celiac disease. It's just a matter of the way it's used is, if those HLA typings are negative, then that is considered good evidence that they don't have celiac disease. So having it doesn't rule it in.
Q. You need to combine the predisposition with the gluten to get celiac disease; right?
A. So most patients have positive serologies for celiac disease, but there is this entity that's referred to in a lot of this literature of what people call "seronegative celiac disease."
But most clinicians would like to see a positive biopsy. They'd like to see a positive tTG. They'd like to see the correct HLA typing. And they'd like to see a response to a gluten-free diet.

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Q. Seronegative celiac disease has been noted in some articles -- rephrase.
Some patients who were diagnosed with seronegative celiac disease have later been reclassified as having olmesartan-associated enteropathy. That's documented in the literature; correct?
A. I think that's -- that may be true, but I did find that to be a very difficult thing to sort out in the papers.
Q. Move to strike from "but" forward.
Coming back to my point, it may be that there are people with a genetic predisposition that has not yet been identified with regard to olmesartan, and when you combine that predisposition with the introduction of olmesartan, they get this condition.
That's possible; right?
A. Yes.
Q. In number 8, you talk about the anemia.
You would agree with me that normocytic normochromic anemia can occur with

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villous atrophy; correct?
A. I tend to think of the classic presentation of villous atrophy associated with celiac disease as an iron-deficiency anemia.
Q. And that can occur with celiac disease; right?
A. So that would be a microcytic anemia with a low iron state. So what -- what the word "normocytic" means that the size -- the average size of the red cell is normal, but in iron-deficiency anemia, the red cells get smaller. And normochromic means that a color measurement is normal.
So, yeah, patients can have a normocytic normochromic anemia and that's -- that's more typical what we call "anemia of chronic disease."
Unfortunately, there was -- I don't recall any statement in here of iron or ferritin level in these patients, which would have been helpful, but one of the strong indicators for upper endoscopy to rule out celiac is, we routinely do that in people who have iron-deficiency anemia. That's a big part of our

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clinical practice is working that up.
So I just commented on it here because I found it surprising.
Q. It doesn't rule anything out, though; right?
A. I don't think so.
Q. Number 9 you talk about 10 of 22 patients having hypoalbuminemia?
A. Correct.
Q. Indicative of protein loss or malnutrition; right?
A. Correct.
Q. And then you point out that the other cases didn't have it, suggesting a highly variable case presentation; right?
A. Correct.
Q. The fact that there can be a highly variable presentation doesn't mean that the condition doesn't exist; right?
A. It doesn't, but, again, if I were to ask you at the end of you going through all of this just for this one case series to define the condition, you wouldn't be able to include iron-deficiency anemia, you wouldn't be able to

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include steatorrhea, you wouldn't be able to include hypoalbuminemia, which are all signs of malabsorption.

So to say it's definitely a syndrome that causes malabsorption, I would not be able to say that that's a written-in-stone component of the syndrome. I was trying to explain that it's very hard to describe what the syndrome is.

Q. Well, one could have malabsorption and not have to have hypoalbuminemia. They could have malabsorption without steatorrhea; right?

A. I suppose, but it's hard for me to conceptualize substantial destruction of a epithelium in the small bowel and not present with some of those findings.

Q. I know you didn't consider the analogy to celiac, but in celiac, the presentations can be highly variable; correct?

A. Correct.

Q. Let's look at number 10, small bowel bacterial overgrowth.

First of all, you say that -- let

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me -- new question.

Number 10 you say small bowel bacterial overgrowth was detected in 12 out of 22 patients; right?

A. Correct.

Q. You acknowledge in the next sentence this could be secondary to a damaged small intestine; correct?

A. Correct.

Q. You then analyze it a little further and say:

"This suggests that other factors could have caused disease in these patients and further supports that the olmesartan use is an association and not a pure cause and effect."

That's what you state; right?

A. Right.

Q. Okay. And those are your words that this evidence supports that olmesartan is an association, not a pure cause and effect, and that's your view here; correct?

A. Correct.

MR. CHRISTIAN: Adam, we have about 10 minutes left.

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BY MR. SLATER:

Q. Are you familiar with --

MR. CHRISTIAN: We just have 10 minutes left.

MR. SLATER: I'm sorry?

MR. CHRISTIAN: I'm just letting you know that we have 10 minutes left on the tape.

MR. SLATER: Okay. Thank you.

BY MR. SLATER:

Q. Give me one second.

On page 737 of the Rubio-Tapia article, the top right corner, the authors point out:

"Finding small bowel bacterial overgrowth in 12 patients is intriguing and consistent with prior observations of association of small bowel bacterial overgrowth and enteropathy in symptomatic patients with celiac disease."

You don't disagree with that statement; correct?

A. No, I don't.

Q. And then further down they say:

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"In this series, the lack of clinical response to oral antibiotics suggests that gastrointestinal symptoms are not explained by the effects of an increased number of bacteria in the small bowel."

And you don't disagree with that statement, do you?

A. So the word "suggest" is not as strong as saying indicate. So it's a suggestion. It's a piece of information, but it doesn't -- it doesn't disprove the notion that this overgrowth is going on and could be contributing to the condition.

Q. Move to strike from "but" forward.

The fact that there was no clinical response to oral antibiotics would cut against that bacterial condition being the cause of the gastrointestinal symptoms; correct?

A. So I'm not trying to say it's the only cause. I'm just saying it could be an exacerbating factor, and clinicians know that treating small intestinal bacterial overgrowth is a daunting task. Some patients struggle with

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this for years and go through all different rounds of antibiotics, and it's very difficult to just eradicate it because we're not even sure if we're treating a pathogen or if we're just treating normal bacteria. It's actually quite a confusing entity.

Q. So it's possible that the patients who were found to have this finding developed the condition in their small intestine as described in the article, including the villous atrophy and the inflammation, and as a consequence or secondary to that, developed small bowel overgrowth. That's possible; right?

A. Yes, but it's also possible they had some other condition that predisposed them to bacterial overgrowth and they just happened to be taking olmesartan.

Q. Move to strike from "but" forward.

As you sit here now, for the 22 patients in the Rubio-Tapia article, you don't have an opinion to a reasonable degree of medical certainty that they have a diagnosis other than olmesartan-associated enteropathy; correct?

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You don't have an alternate diagnosis to a reasonable degree of medical certainty for any of these patients; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: Well, as I indicated before, I do feel that their follow-up article calls into question some of the conclusions of this study, but I haven't had the opportunity to know anymore than what's in these two articles. I don't have access to patient identifiers or to discussions with the authors.

BY MR. SLATER:

Q. Move to strike.

As you sit here now, you're not giving an opinion to a reasonable degree of medical certainty as to an alternative diagnosis other than olmesartan-associated enteropathy as the cause of these patients -- these 22 patients' clinical presentation; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I don't have enough information to give an alternative

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explanation.

BY MR. SLATER:

Q. You comment on, in number 11, the evidence of collagen deposition in 7 of the 22 patients?

A. Right.

Q. Right?

A. Yes.

Q. The literature talks about a spectrum of clinical and histopathologic findings; correct?

A. In what condition?

Q. The findings on biopsy.

A. In general or in this?

Q. The spectrum reported in the literature for this condition; correct?

A. Yes.

Q. Okay. There's a spectrum of histopathologic findings with people with celiac disease; correct?

A. Correct.

Q. Let's go to number 13, the colonoscopies that you said were done on 13 of 22 patients.

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A. Yes.

Q. First of all, these were patients that were given colonoscopies or endoscopies as part of clinical decision-making by doctors who were trying to help these patients in a clinical setting; correct?

A. Correct.

Q. You point out that there were 7 patients who were found to have microscopic colitis if we look at the table, Table 2; correct?

A. Correct.

Q. You say in your report, and putting aside the difference between 7 or 5 patients, that in the text of the article it is stated that those patients who had microscopic colitis, presumably meaning there was no endoscopic evidence of disease.

That's what you state; correct?

A. Yes. I had to write that because they didn't define for them what the term "microscopic colitis" meant. I had to assume that's what it means.

Q. Move to strike after "yes."

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You're not suggesting that endoscopies weren't done on those 7 patients, are you?

A. No, I'm not.

MR. CHRISTIAN: Objection. Form.

BY MR. SLATER:

Q. Single one of those patients who was found to have colitis was also found to have disease on endoscopy with either partial or, in most cases, total villous atrophy; correct?

A. You cut out at the beginning of the question. I didn't hear it exactly.

Q. For all 7 of the patients on Table 2 who were found to have colitis, every one of them was found to have either partial or, in most cases, total villous atrophy on endoscopy; correct?

A. Yes.

MS. WADHWANI: Adam, sorry to interrupt. There's only two minutes of tape time left.

MR. SLATER: All right. Let's break.

THE VIDEOGRAPHER: Time now is

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12:14. We are going off the record. This is the end of Disk No. 2.

(Whereupon, at 12:14 p.m., a luncheon recess was taken.)

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AFTERNOON SESSION

(12:55 p.m.)

KEITH T. WILSON, MD

called for continued examination and, having been previously duly sworn, was examined and testified further as follows:

EXAMINATION (CONTINUED)

THE VIDEOGRAPHER: Time now is 12:55. We are back on the record. This is the beginning of Disk No. 3.

BY MR. SLATER:

Q. Okay, Doctor. I'm looking at your report, page 3, number 14, and I want to ask a couple questions about some of the things you point out.

First of all, you're referring to with the article where they talk about the fact that some therapies that had been used with the patients before they came to the Mayo Clinic did not apparently benefit them; right?

A. Correct.

Q. And, for example, if you look at page 735 of the study?

A. Yes.

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Q. It talks about the fact that 20 of the patients were on a gluten-free diet for months and didn't have any apparent clinical benefit; right?

A. Correct.

Q. And then it talks about the fact that steroids were used with 20 of the patients, and they apparently didn't have apparent clinical benefit; correct?

A. Correct.

Q. And then it points out in the next paragraph:

"Clinical response was observed in all 22 patients after suspension of olmesartan."

Correct?

A. That's what is stated, but that's not a result, considering that in the patient methodology section, they stated that they only included patients who had improved off of olmesartan.

Q. Move to strike the tail end of that answer.

The patients in this study, all

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22, had a clinical response when they stopped taking olmesartan; correct?
A. Yes.
Q. That's what is documented in this study; correct?
A. Correct.
Q. And, again, these were patients who were clinical patients who were not able to be successfully treated, and it was only looking back and figuring out the connection to olmesartan that was the unifying feature, that they got better when they got off olmesartan; right?
A. That's what they stated.
Q. The fact that all 22 patients had a clinical response to stopping olmesartan, that is -- that's important evidence; right?
A. It is, except for the fact that it's circular reasoning because in order to be included in the study, they had to have improved off of olmesartan. So they're not telling us how many people they saw with complex presentations that were negative for celiac disease that actually had this condition.

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Q. Move to strike after "it is."
These patients, it says, didn't need other medications to control their symptoms, that the clinical response was achieved just by suspending the drug. That's what it says; right?
A. Right.
Q. That is -- that's referred to as a positive dechallenge, meaning the drug was stopped and the symptoms went away. That's what a dechallenge is when it's positive; right?
A. That's not what was done here. This is just a retrospective story talking about all different patients, and there's no -- there's nothing systematic here. There's no protocol for dechallenge.
Q. So this study you don't -- you don't weigh this study at all because it was not a systematic controlled study.
Do you think that this study should not be considered?
A. No, I weigh it. I think it should be considered.
Q. The fact that these patients recovered and had clinical responses to getting

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off the drug, that is significant evidence that weighs towards causation; correct?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: Well, they didn't write that. They just said that this study did not show causation. They specifically and explicitly stated that they had not shown causation, that they had shown an association.
BY MR. SLATER:
Q. Move to strike.
First of all, Doctor, we'll get to that, but that's not what they say. We'll get there, but we both know that's not what it says, but we'll get there in a minute.
MR. CHRISTIAN: Objection. Form.
BY MR. SLATER:
Q. I promise.
One of the Bradford Hill criteria is cessation of exposure; right?
A. Yes.
Q. When the person -- rephrase.
When these patients stopped taking the drug and got better, that fits with

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cessation of exposure; correct?
A. In the most simplistic interpretation. However, this was not a controlled study in any form.
Q. Assuming that those 22 patients actually stopped taking olmesartan and their clinical condition responded to that, as reported in the study, assuming that to be true, that is significant evidence of causation and fits within the Bradford Hill criteria for cessation of exposure; correct?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: No, I don't agree because it's -- it was not a controlled study, as I stated.
BY MR. SLATER:
Q. So you completely throw aside the fact that all 22 patients are reported to have had a clinical response to ceasing the drug because this was not a controlled study?
Is that your testimony and that's the standard methodology you're applying here?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: I don't completely

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throw it aside. I said their conclusions need to be tempered with skepticism because we know from their 2010 paper that there were other patients that were on olmesartan that didn't get better with discontinuation of the drug.

BY MR. SLATER:

Q. With regard to the 22 patients -- well, one second. Move to strike.

With regard to the 22 patients that are discussed in this article, if it's true that they got off the drug and had a clinical response to that, that fits the cessation of exposure Bradford Hill criteria and would be substantial, significant evidence of causation, if it's accurate; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I think I've already answered that my concern is that it's not like all these patients came in and a specific protocol was employed with, here's our strategy for removing the drug and here's the way we're going to follow them and here's the frequency

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of follow-up, and these are the times where we're going to check their labs and these are the times where we're going to check their endoscopies.

It's all just a retrospective story. You just can't make anymore of it than that.

BY MR. SLATER:

Q. If this had been a controlled study and the dechallenges were done on some sort of a protocol, then you would think this was very significant evidence of causation; right?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: Plus, the study is underpowered. So you would have to randomize people to dechallenge versus not and follow them over time because some people might spontaneously get better, and you would need to control for as many things as possible and you would need a lot more than 22 patients.

BY MR. SLATER:

Q. So your methodology is, unless it's a randomized controlled study, you give very

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little weight to the results of the study; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I give it some weight, but only in the context of what it is. It's Level IV evidence. So I don't say that it should be thrown out. I'm just saying that it is what it is.

BY MR. SLATER:

Q. My question is this: Because it's not a randomized controlled study, you give very little weight to the results and findings and data from this study; correct?

MR. CHRISTIAN: Object.

BY MR. SLATER:

Q. Do I understand your methodology?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: Could you define what you mean by "weight"?

BY MR. SLATER:

Q. When you put all the evidence onto the scales to try to form an opinion as to whether or not olmesartan can cause this enteropathy condition in some patients and you

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look at the results of this study, because it's not randomized controlled, you think that's a very minor factor in the overall analysis; correct?

A. What's a minor factor?

Q. Something that won't have a significant impact on your opinion.

A. My opinion of this study is that this is a reasonable description of 22 patients that they saw, retrospective summary, a write-up of various patients that came. Sort of like a novel, but not something where they set out to test a hypothesis or where they can provide biologic plausibility or they can really give any specific guidelines. It's just a fairly nice write-up of a description of 22 patients.

So I don't throw it out completely. I just feel like, as I've stated repeatedly, it's Level IV evidence.

Q. I'd like you to assume for purposes of my question that the 22 patients, when they got off of olmesartan, they had the positive clinical response described in the article. I'd like you to assume that occurred.

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A. Okay.
Q. That is significant evidence; correct?
MR. CHRISTIAN: Object.
THE WITNESS: I'm sorry. You broke up for the first 10 seconds of that.
BY MR. SLATER:
Q. You assume that the 22 patients, as reported, got off of olmesartan and had the positive clinical response described in the article.
If it's true that that occurred as described, that is significant evidence of causation; correct?
A. I've already answered that. It is not significant evidence of causation.
Q. Well, that's because you think it's not randomized or controlled?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: That's one reason.
BY MR. SLATER:
Q. Well, the reason you want to randomize or control is to have a systematic

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approach to make sure that the -- that getting off the drug is actually what caused the clinical response; right? You're trying to be sure that there's a cause and effect relationship.
Do I understand that?
A. Yes, that would be the best level of evidence, but there could be something intermediate where all the patients are lined up in a row like horses starting in a race and you say, okay, we're going to ring the bell and this is the protocol. And everybody is going to be followed in a certain way and we're going to follow people at certain intervals, and these are the tests that we're going to get. And then we're going to have a nurse call you once a month to check on your symptoms, see what's going on. We're going to measure your weights. We're going to do all these things.
There's no protocol. It's standard and clinical that there has to be a study protocol. There is no study protocol here.
Q. Okay. And that's the reason why you discount the results here; correct?
A. Correct.

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MR. CHRISTIAN: Objection. Form.
BY MR. SLATER:
Q. I'd like you to assume that despite the fact that there was no protocol. There's no randomization. This was not a controlled study. Because as we know, these were actually patients being treated by real doctors who actually do treat these conditions.
That despite the lack of control or randomization, these patients actually did have a positive clinical response to getting off the olmesartan, okay?
MR. CHRISTIAN: Objection. Form.
BY MR. SLATER:
Q. If that is so, that is significant evidence supporting causation; correct?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: So that's a two-part question.
I think the first -- answer to the first part of the question is, I will give credit that they have described what they think they've observed, but I will

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not say that this paper alone is enough to say that there is significant causation. Because if there had been, they would have made that conclusion and they did not.
BY MR. SLATER:
Q. Move to strike from "because" and we'll get to that. I promise we will get to that.
MR. CHRISTIAN: Objection. Side bar.
BY MR. SLATER:
Q. The article talked about the fact that there was not a finding of intraepithelial lymphocytosis; correct?
A. Well, some of the patients had that. I just document in my report that it was surprising that 8 out of 22 did not have increased intraepithelial lymphocytes.
Q. It is possible that the steroids that these patients took reduced the inflammation and, thus, reduced the prevalence of intraepithelial lymphocytosis.
That's possible; right?

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A. Except it's -- sure, it's possible, except for the fact that they specifically said they didn't have a response to steroids.

Q. Well, they could have had a response in terms of how the intestinal architecture appeared, but not have actually felt clinically better; right?

You could -- you could not feel better, even though you don't have intraepithelial lymphocytosis; right?

A. That's a double negative. I'm sorry. You're going to have to rephrase that. I can't -- I can't process that one.

Q. (Laugh).

The steroids could have made the pathology look better, but the patients might not have felt clinically better.

That's possible; right? That's a possible outcome of using the steroids; right?

A. Except for the fact that 15 of the patients had severe villous atrophy and 7 had partial. So it's pretty hard to say that the steroids were working on one thing and not the

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other because the immunopathogenesis that's assumed here is that it's activation of these alleles that leads to the epithelial destruction. So it's kind of hard to say that they shouldn't relate to each other.

And that the paper is not well enough written to tell us whether it's the same people that had less alleles that also had less atrophy. That would be nice to know, but it's not written to that level of depth.

Q. Let's look at number 15. The fact that 17 of the 18 patients tested had histologic recovery; right?

A. Right.

Q. And on Table 2, the 18th patient, who's patient number 2, had improvement and had gone from having total villous atrophy to focal partial villous atrophy at 54 days; correct?

A. Right.

Q. In the histologic presentation; correct?

A. Right.

Q. The rate of histologic recovery with celiac disease is variable; correct?

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A. Yes.

Q. If I understand correctly, one of your criticisms is that there were not follow-up biopsies beyond those listed; correct?

A. Right.

Q. Again, these were patients in the real world being treated. They were improving and getting better.

So you would not expect to do multiple follow-up biopsies on patients who were improving and resolving their symptoms; right?

A. I would agree with that.

Q. You would agree with me one possible cause of the villous atrophy described in this article was the olmesartan.

That's a potential cause of that; right?

A. A potential cause, sure. Just like it could have been other things with these patient, as I listed.

Q. In these patients -- I think we went through this before -- you can't point to another cause to a reasonable degree of medical certainty for the villous atrophy described in

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this article; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: Well, we discussed earlier today that it was my take on the follow-up paper that some of these patients may have actually had occult celiac disease.

BY MR. SLATER:

Q. May have what?

A. May have had occult celiac disease.

Q. You're not saying they had occult celiac disease to a reasonable degree of medical certainty, though.

We've established that; right?

A. Well, that's the flaw of the Cartee paper. It's published in a non-PubMed journal and is a very poor review. It's not really very scientific in the way it's presented. It's impossible to know what was discussed.

Q. Move to strike.

The answer is I'm correct; right?

A. Correct to what? Why don't you restate the question.

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Q. You're not offering an opinion to a reasonable degree of medical certainty that these patients had occult celiac disease, any of them?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I'm not willing to say that none of them had that.

BY MR. SLATER:

Q. You're not willing to say to a reasonable degree of medical certainty that any of these patients did have occult celiac disease.

You're speculating maybe some did, but you're not saying to a reasonable degree of medical certainty they did; right?

A. I think at the time that Dr. Murray wrote this paper, that was the evidence that he had. I'm just saying that the follow-up paper strongly suggests either it's some of these patients or very, very similar patients, some of them were later found to have celiac after they had their drug stopped.

Q. Very simply. With these 22 patients, you're not saying that their villous atrophy, as documented, was to a reasonable

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degree of medical certainty caused by anything other than olmesartan; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I'm unable to say because there's not enough information.

BY MR. SLATER:

Q. You're not opining that it's a coincidence that all 22 of these patients had villous atrophy and all 22 had a clinical response to withdrawal of olmesartan. You're not saying that's a complete coincidence, are you?

A. It can't be a coincidence because those were the inclusion criteria for the case write-up.

Q. Okay. The likelihood is that for the 22 patients who had villous atrophy, who had the severe diarrhea, the weight loss, and then resolution of the symptoms over time or, in the one case, improvement over time after the withdrawal of the drug, the likelihood is that they were suffering from something caused by the same syndrome; correct?

MR. CHRISTIAN: Objection.

BY MR. SLATER:

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Q. That's the likelihood; right?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: "Something caused by the same syndrome." That's really vague. I'm sorry, but I don't know what that means.

BY MR. SLATER:

Q. I'll ask it differently.

With regard to the 22 patients, the likelihood is that the cause of their condition was the same. That's the likelihood; right?

A. Because they bias this case series by saying, we looked for patients that got better off of olmesartan, but there's clearly patients that they had that didn't get better off of olmesartan. So their features were completely different.

Q. As to the patients who got better when they got off of olmesartan, the likelihood is that the olmesartan was causing the syndrome, the diarrhea, the villous atrophy; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I've already stated

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that it appears that there's an association, but because it's retrospective and the study was biased in terms of who they selected, I can't use the word "caused."

BY MR. SLATER:

Q. Move to strike from the word "but" forward.

Based on the information that is available in the study, in this article, the likely cause of these 22 patients' clinical symptoms, their villous atrophy, was the olmesartan; correct?

MR. CHRISTIAN: Objection. Form.

BY MR. SLATER:

Q. Based on that information?

MR. CHRISTIAN: Same objection.

THE WITNESS: I think you've asked me the same question multiple times, and I've answered it the same way each time.

BY MR. SLATER:

Q. The reason you won't say yes to causation is because it was not a controlled

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study. Do I understand correctly?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: That's one reason, but I already talked about that, so there's no placebo group. But also that there's no protocol, there's no study protocol. And because it's retrospective, the information available is patchy.
So that if I asked -- if I were asked to define the syndrome that's described here, the only two commonalities are that they had villous atrophy on their biopsy, because they all had either partial or total, and that they improved off of olmesartan because they selected the patients that improved off of olmesartan.
But all of the other features -- weight loss, gastric involvement, colonic involvement, steatorrhea, anemia, hypoalbuminemia -- none of those things are consistent. There are more things that are inconsistent than things that

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are consistent.
BY MR. SLATER:
Q. In fact, the picture here is analogous to celiac where you don't have the same clinical presentation for all patients, but gluten is the cause along with the person's predisposition for their clinical presentation and for their histopathologic presentation; right?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: I don't think that's relevant because celiac disease does not cause colitis, and some of these patients had colitis. We know that celiac disease does not cause colitis.
BY MR. SLATER:
Q. In the sense that there's a varied presentation with celiac, there's a consistency between the two; correct?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: I think that the presentation with celiac disease can be more easily summarized in textbooks because 1 percent of the population has

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it. So then when you're summarizing what the condition is and how to work it up, you're dealing with 3 million Americans that have celiac disease versus in this you're talking about less than a hundred cases in the world's literature. So, therefore, I cannot compare the two.
BY MR. SLATER:
Q. Let's look in the article page 735. The discussion, the second paragraph says:
"We acknowledge that this case series lacks all the information necessary to prove causality but, rather, reflects an association."
You see that statement?
A. Yes.
Q. You agree with that statement; correct?
A. Yes.
Q. Okay. Now, you see the word "prove"?
A. I see it.
Q. You realize that in this litigation we don't have to prove something. We

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just have to show more likely than not.
Are you aware of that?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: I'm not an attorney. So that's not my concern.
BY MR. SLATER:
Q. Okay. They state that there was no deliberate rechallenge because of the life-threatening nature of the syndrome; correct?
A. Yes.
Q. That was a reasonable clinical decision by the doctors treating these patients; right?
A. Well, the doctors treating the patients weren't aware there was a syndrome. You yourself said it was real world doctors taking care of patients. So they made a clinical judgment in those particular patients that they didn't want to restart this medication, just like they might have held other medications.
Q. Once these doctors realized that the patients had gotten better off of olmesartan, they felt it would be unsafe to put them back on olmesartan to rechallenge them due to the

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severity of the condition.
That was a reasonable clinical decision; correct?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: Potentially, yes, but the thing that I find confusing about your argument and about this paper is, I don't believe for sure that all 22 patients were -- were cared for by Dr. Murray. I don't really know.
So it could be that other members of their group took care of these patients. So I don't have the impression they all sat down and said what they think they needed to do. I think individual physicians made their own decisions.
BY MR. SLATER:
Q. It says right here no deliberate rechallenge test with olmesartan was undertaken.
That means that once they figured out this association, they said, okay, we're not going to put them back on the drug to quote/unquote prove this because it would be too

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dangerous.
That's what that means; right?
A. Yes.
MR. CHRISTIAN: Objection. Form.
THE WITNESS: That's what they wrote.
BY MR. SLATER:
Q. And that's a reasonable clinical decision; right?
A. I think if I ever thought that anybody had a reaction of some sort to a medicine I would -- even if it was really not even certain, I wouldn't take the chance because there's so many other medications we can use for all the conditions we work with.
Q. They talk about two patients reporting anecdotally that their symptoms worsened when they restarted olmesartan before the potential association was recognized.
That's what the patients told them; right?
A. Correct.
Q. Is there any reason to disprove the patients that that's what happened?

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A. No, but anecdotally, I mean, we're not talking about science here. We're just talking about a story.
Q. Move to strike from "but" forward.
This also indicates two patients experienced improvement when olmesartan was stopped when they were hospitalized for dehydration and hypotension and worsened in the weeks following discharge and reintroduction of olmesartan.
You see that?
A. Yes.
Q. Okay. That is evidence, as described, of a positive rechallenge. They were put back on the drug and they got sick again.
That's what is being described there; correct?
A. To me, a rechallenge has to be controlled.
Q. You believe that rechallenge for -- rephrase.
You define rechallenge only to include a controlled rechallenge in your

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methodology?
A. So by "controlled" I mean there needs to be a study protocol. There needs to be close observation of the patient. There needs to be prescribed parameters that are going to be followed.
It can't just be, we restarted the medicine and they felt bad. We need to know, did their atrophy come back? How many bowel movements a day were they having? What happened to their -- did they start having fecal fat again? Did they become anemic? I mean, there's nothing like that here. If this were real data, it would be in the results section of the paper, not in the discussion.
Q. So there is no rechallenge that you will -- rephrase.
So your methodology is, if somebody was put back on the drug, unless it was done in a controlled way pursuant to a study protocol, you will not rely on that in determining causation; correct?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: I would say that in

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general terms that would be true.
BY MR. SLATER:
Q. Do you agree with me that based on your reading of the overall literature that there are patients who were on olmesartan, got severe diarrhea, dehydration, and weight loss, got off olmesartan and got better, and then went back on olmesartan and their symptoms came back?
Do you agree that that has happened to some patients?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: I believe that that has been described in some of these papers, but only in the case series and not in any controlled fashion.
BY MR. SLATER:
Q. Move to strike from "but" forward.
My question is: Do you believe that that -- rephrase.
In drawing your assumptions as an expert in this case, are you assuming that for some patients that has actually occurred?
MR. CHRISTIAN: Objection. Form.

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THE WITNESS: What? Can you restate what the "that" refers to?
BY MR. SLATER:
Q. I just asked you about that there are some patients who are on olmesartan, developed severe diarrhea, dehydration, weight loss, got off the olmesartan, their symptoms improved or got better, and then later they were put back on the olmesartan and they got back to the same baseline of being sick again.
Do you believe in drawing your assumptions that that has happened to some patients?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: There are -- I think there are some scattered reports of that, but nothing controlled.
BY MR. SLATER:
Q. Move to strike from "but" forward.
Are you aware of any patients who are in a randomized controlled study who had a positive dechallenge off of olmesartan and then were later put back on olmesartan and had a

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positive rechallenge in the context of a controlled randomized study?
A. There have never been any randomized controlled trials related to olmesartan in terms of once this association was recognized. I'm not and I don't have access to the original toxicity testing and such that was done in patients during the Phase I and Phase II trials before the drug was approved.
Q. My question is: Do you know of any patients who in a randomized controlled trial on olmesartan developed symptoms consistent with olmesartan-associated enteropathy, had a positive dechallenge, meaning they got better off the drug, and then were put back on the drug later and got sick again?
A. No, I'm not.
Q. Are you aware of any patients like that?
A. No.
Q. If there were any such patients like that, would that be -- would that be significant to you in forming your opinions?
MR. CHRISTIAN: Objection. Form.

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THE WITNESS: It would all depend on the quality of the study, the power of the study, what type of information they collected. It can't just be patient got better, patient got worse. Those aren't scientific terms.
BY MR. SLATER:
Q. If such a dechallenge and a rechallenge were documented in a randomized controlled trial, in and of itself, would that be of significance to you? Something you would want to look closely at and consider giving significant weight to?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: Yes.
BY MR. SLATER:
Q. If Daiichi was available -- rephrase.
If Daiichi and their lawyers who hired you were aware of any such cases, would you have liked to have been provided those so you can consider that in forming your opinions?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: So you just jumped

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from RCT to the cases. So that's a different thing.
BY MR. SLATER:
Q. No, I actually didn't, but I'll be -- I'll try to be as rigorous as you are with the word "cases."
If such patients existed and were known to Daiichi and their lawyers who hired you, would you have wanted to see that data?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: "Such cases," please define.
BY MR. SLATER:
Q. Such cases as I just described. A patient in a randomized controlled trial on olmesartan, who had symptoms consistent with olmesartan-associated enteropathy, who got better off the drug and then got sick again on a rechallenge.
A. I don't think one patient would mean anything, but if there were many patients and it was all controlled and it were peer-reviewed, then I'd be interested in looking at it.

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Q. So if that type of a patient -- rephrase.
So if that scenario actually exists and is known to Daiichi and their lawyers, you wouldn't even want to see it. It wouldn't even matter to you?
MR. CHRISTIAN: Objection. Form.
BY MR. SLATER:
Q. Is that your testimony?
MR. CHRISTIAN: Same objection.
THE WITNESS: I don't know whether they have controlled data on patients. I only know what's in the literature. That's what I was asked to do.
BY MR. SLATER:
Q. That's my point. If they knew about it, your testimony is you wouldn't want to see it anyway because it wouldn't be of any significance to you?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: I'm really unable to answer that because, frankly speaking, I don't know what internal drug company

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documents look like, but my supposition is, they don't reach the level of evidence of what I would expect from a peer-reviewed paper. It would just be some -- I don't even know what it would be because I haven't seen it.
BY MR. SLATER:
Q. Really my question is pretty simple.
If there's a patient in a randomized controlled trial as I described, is it your testimony you're fine not even seeing that, it's not something that would be of any significance to you sight unseen, you don't even need to see it?
MR. CHRISTIAN: Objection. Form.
BY MR. SLATER:
Q. Is that true?
MR. CHRISTIAN: Same objection.
THE WITNESS: I don't know one. You just said "a patient." That's the singular form. I don't think one patient is worth trying to make any conclusions about causation from.

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BY MR. SLATER:
Q. Have you done any power calculations?
A. In my life? Sure.
Q. Or calculations in this case. I didn't see any in your report.
MR. CHRISTIAN: You cut off the first part of your question.
BY MR. SLATER:
Q. See any power calculations in your report. Did you do any?
A. What would you have liked me to do a power calculation on?
Q. I don't really understand why you would ask -- answer me with that question, but we can -- we can play it out if you want.
A. Well, I was supposed to --
Q. I can do that well for you, Doctor. I'll ask it again.
I read your report. I didn't see you do any power calculations.
Did I miss it? Did you do one?
A. No, I did not.
Would you like me to expound on

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what a power calculation is, or would you like to define it for me?

Q. No, I think I know what it is. You don't need to expound. I want you to get to dinner with your wife. So let's not expound. Because if you expound, I'll tell her you were late because you were expounding.

A. She knows that I do that.

Q. I bet she does.

Okay. Let's look now back at the discussion on page 735. The authors state:

"Resolution of the presenting symptoms and subsequent histologic improvement after suspension of olmesartan, in the absence of clinical evidence of other diseases associated with enteropathy, suggest that the association is not likely to be due to chance."

Do you see what I just read?

A. Yes.

Q. I didn't see you quote that language in your report. Did you?

A. No, not to my memory.

Q. I'm sorry. What did you say?

A. I -- (reviewing document).

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Q. You can look at number 17 on page 4, your point 17. I see you quoted the sentence at the top of the paragraph.

A. Uh-huh.

Q. You didn't quote the last sentence I just read to you about not likely being due to chance; right?

A. Right.

Q. If the association is not likely to be due to chance, then it is likely that there is a causal relationship; right?

A. No.

MR. CHRISTIAN: Objection. Form.

THE WITNESS: It doesn't say that.

BY MR. SLATER:

Q. Yeah. Well, I'm talking about the meaning of the English language now with you.

If it's not likely due to chance, meaning it's not just by chance, then it is more likely that there is a causal relationship.

That's what that means in English language; right?

MR. CHRISTIAN: Objection. Form.

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THE WITNESS: So when we think about statistical analysis, we -- we use P values, which represent the probability that something is due to chance alone.

So I don't know if you knew that but, for example, a P value of .05 means that --

BY MR. SLATER:

Q. (Laugh).

A. -- 5 out of a hundred times the result could be just due to chance. P value of .01 would mean 1 out of a hundred times it could be due to chance. So it's a probability value.

So I'm very familiar with the concept of something being likely or not likely to be due to chance. I didn't cite it because I didn't think the sentence added anything.

Q. Doctor, let's look at what you did do. And you know what? You're probably right. Although, actually, I don't think you know what a P value is, but we'll talk about it another time.

MR. CHRISTIAN: Object to the side bar.

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BY MR. SLATER:

Q. We'll go to it another time. You asked me. You made fun of me. Maybe we both don't know. Maybe we're equally noninformed on it, but anyway --

MR. CHRISTIAN: Objection. Just ask your questions, Adam.

BY MR. SLATER:

Q. -- in your report number 17 -- I'm sorry. I can't hear.

You wrote in number 17 --

MR. CHRISTIAN: I said move on in your questions.

BY MR. SLATER:

Q. You wrote it was necessary -- is someone talking? Is someone talking?

MR. CHRISTIAN: Go ahead. I said go ahead and ask your questions. Go ahead.

MR. SLATER: Isn't that what I'm doing?

BY MR. SLATER:

Q. You felt it necessary and relevant to quote in paragraph 17 on page 4, you

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quoted where they said they acknowledge the case series lacks all the information necessary to prove causality but, rather, reflects an association.

You quoted that language in your report; right?

A. Yes.

Q. You quoted it because you wanted to point out that the authors' conclusion was that it showed an association, didn't prove causation. That's why you quoted it; right?

A. Correct.

Q. You didn't quote the bottom line in the paragraph where they said that the association is not likely to be due to chance.

You didn't quote that; correct?

A. Because --

MR. CHRISTIAN: Object to form.

THE WITNESS: I didn't because they're still talking about an association. So I didn't think it added anything.

BY MR. SLATER:

Q. Move to strike from "because"

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forward.

If we're just going by their conclusion and quoting their language, if they say it's not likely to be due to chance, that means it's more likely that there is a causal relationship?

MR. CHRISTIAN: Objection.

BY MR. SLATER:

Q. Correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: Well, wouldn't they have written it the way they you just said if that's what they thought?

BY MR. SLATER:

Q. Move to strike.

That's what the word means in the English language; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: That's your interpretation, not mine.

BY MR. SLATER:

Q. If it's not likely due to chance, it's more likely that it's not a chance association, but there's actual cause and effect; right?

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A. No.

MR. CHRISTIAN: Objection. Form.

BY MR. SLATER:

Q. Okay. Olmesartan-associated enteropathy, as described in the literature, is an uncommon adverse drug effect; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: It's rare, to say the least. Yes, it's very rare.

BY MR. SLATER:

Q. A definition of "rare" something that's peer-reviewed where the word "rare" is defined?

A. That's a good point.

That word is thrown around. I would say that there are some estimates in some of these papers that we haven't discussed that use surrogate markers that suggest that it's very uncommon.

Q. Very what?

A. Very uncommon.

Q. Okay. All right. So I'll use that language.

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You would agree with me that olmesartan-associated enteropathy, as described in the literature, is an uncommon or a rare adverse drug effect; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I don't know if I can say "adverse drug effect" because effect implies that there's more certainty about it. I would say association.

BY MR. SLATER:

Q. This was never prospectively studied by the manufacturer; correct?

A. I don't know.

Q. As far as you know?

A. I don't know.

Q. You haven't seen anything suggesting that Daiichi attempted to prospectively study the issue; right?

A. I'm not -- I don't know anything about Daiichi and what they do. I've never talked to anybody from their company.

Q. Anything indicating anybody has prospectively studied this question?

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A. And the reason is that you would need to follow such a huge number of patients to potentially find any that it would be unfeasible to do such a prospective study.

Q. Right. So you trying to say that you can -- that causation is not proven because a controlled prospective study was not done, you'd acknowledge that you wouldn't expect such a study to be done; right?

A. You could prospectively describe. For example, you could look at some -- I mean, I'd have to sit down and think about it. A de novo study would be tough. There could be some other ways of, for example, the way they went back and reanalyzed the data from the ROADMAP study. Albeit that has the caveat that that wasn't their original end point, but they went back and looked at that where you have a huge number of patients. That sort of data.

Q. Do you rely on the ROADMAP study in part for your opinions?

A. It's one of the -- one of the articles that I thought was worth considering.

Q. Calculation -- rephrase.

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In your methodology, did you rely in part on the ROADMAP study data as supporting your opinion?

A. Yes.

Q. Was the ROADMAP study data important to you in forming your opinion?

A. It was somewhat important.

Q. Where an adverse drug effect or, as you want to call it, an adverse drug association has not been prospectively studied, as it has not been prospectively studied here with olmesartan, case reports of clinical results can be very significant in providing information about a potential adverse drug reaction; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I'd say that that should be considered, but there -- there are other pieces of evidence that I discussed in my report that didn't select the cases based on the end point and then working backwards but, rather, started with looking at all people with diarrhea or all people with other conditions and then trying to follow through and make

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calculations.

BY MR. SLATER:

Q. Move to strike from "but" forward.

Are you aware that those who are experts in the field who are celiac specialists who see the most complex seronegative celiac cases or the most serious unclassified sprue cases, etc., that they accept that olmesartan causes sprue-like enteropathy or olmesartan-associated enteropathy in some number of patients?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: So having read the expert reports of the people that I listed, I became aware that there are some people that think that, but I don't think that's very scientific.

BY MR. SLATER:

Q. Move to strike from "but" forward.

Are you aware that the prevailing scientific consensus among those clinicians who actually evaluate and treat this condition is

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that olmesartan causes this condition in some number of patients? Will you acknowledge that?

A. No.

MR. CHRISTIAN: Objection. Form. Go ahead.

THE WITNESS: I don't -- I don't acknowledge that. The only information I have on that is a couple of these expert reports.

BY MR. SLATER:

Q. Well, you've read multiple articles where the articles say that olmesartan causes this condition, that olmesartan induces this condition.

You've seen that in multiple articles; right?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I don't think it's convincing.

BY MR. SLATER:

Q. Move to strike.

You've seen that that language exists in multiple peer-reviewed articles; right?

MR. CHRISTIAN: Objection. Form.

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BY MR. SLATER:
Q. I'm not asking if you agree. I'm asking if you've seen it.
A. I don't know about the word "induced."
Q. You don't -- you haven't seen the word "induced"?
A. I know --
Q. Olmesartan-induced enteropathy? You haven't seen that in any of the articles?
A. It's possible, but it doesn't come to my mind.
Q. Carefully read these articles to see what language was used?
A. Of course I did.
Q. Induced means caused; right?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: So here's the way I would define "induced" in my own research.
I take cells and put them in a dish. I add H. pylori. I measure an output from the cells and I write "H. pylori induced an increase in

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production of such and such factor." I've published many papers writing things like that.
That's not the same thing as somebody perhaps using the word "induced" in a discussion, but I don't recall the use of that word. Perhaps it's buried in one of these discussion sections.
BY MR. SLATER:
Q. Do you know what the head of pharmacovigilance at Daiichi Sankyo during the time period when this was all being discovered, do you know what he thinks olmesartan-induced enteropathy means?
A. No, I do not.
Q. Would it be of any interest to you to know that, or it would be irrelevant to you?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: I don't know the inner workings of a drug company. So I don't know the hierarchy. I don't know what -- if something existed like that, I don't know what the quality of the

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evidence is. I would just be speculating.
BY MR. SLATER:
Q. Would you like to understand all those things so you'd understand what the company that actually sold and monitored the drug, what they actually know and think? Would you have liked to have known that?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: I don't think that it's really relevant to the task that was put before me of assessing the medical literature and thinking about the science behind that because internal documents are not -- they're not peer-reviewed. I don't know anything about how they're constructed or -- or anything.
BY MR. SLATER:
Q. Your comment 19 on page 4 of your report says that -- talks about mechanism, the concept of mechanism; right?
A. Right.
Q. You do not need to know the mechanism of an association; correct?

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MR. CHRISTIAN: You might need to restate that. We missed the middle part.
BY MR. SLATER:
Q. You do not need to know the mechanism in order to recognize that there is clinical evidence of an association; correct?
A. I suppose if the clinical evidence were compelling with a lot more than less than a hundred patients that have been described, you could reduce your desire to know about that. However, many other conditions, we have a much better handle on what the biological mechanisms may include. Here we have none.
Q. You do not need to understand the mechanism at a molecular level to have a biologically plausible mechanism for a condition; correct?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: No, I don't agree to that.
BY MR. SLATER:
Q. In order to have a biologically plausible mechanism, you have to understand the mechanism at the molecular level?

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A. I think that you should understand the -- at the pathophysiologic level and at the molecular level, you should have some understanding of that, yes.
Q. Some understanding. For example, if, if -- let me ask you this question.
If those who believe that olmesartan causes an immune-mediated response that causes cellular changes in the intestine that leads to villous atrophy, inflammation, and the clinical symptoms that have been reported, if that is accurate, that is a biologically plausible mechanism; correct?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: But there is no evidence of how it's activating the immune response.
BY MR. SLATER:
Q. Is true that is a plausible biological mechanism; correct?
A. You cut out at the beginning. I couldn't hear that.
Q. I moved to strike and then I said: If that is true, that is a plausible

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biologic mechanism; correct?
A. I just said, if there's no understanding of how the immune response gets activated, I'm not certain there is evidence that the immune response gets activated.
Q. I move to strike.
Here's my question.
I want you to assume that olmesartan causes an immune-mediated response in the intestine which leads to inflammation, villous atrophy, the other findings that have been seen in the studies, and the clinical symptoms that have been reported. I want you to assume that to be true.
If so, that would be a plausible biologic mechanism; correct?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: That's not -- that's -- first of all, that's just a speculation. It's not a biological mechanism.
BY MR. SLATER:
Q. Move to strike.
If that is factually true, that

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is a plausible biologic mechanism; correct?
MR. CHRISTIAN: Same objection.
THE WITNESS: That does not have enough depth.
BY MR. SLATER:
Q. If it's true that olmesartan causes an immune-mediated response that causes cellular changes in the intestine which leads to inflammation, villous atrophy, and the other histopathologic findings that have been reported and leads to the clinical symptoms that have been reported, if that is true, that is a plausible biologic mechanism; correct?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: I think I've already answered it.
MR. SLATER: Question, please?
(The reporter read the record on page 212 lines 6-13.)
MR. CHRISTIAN: Objection. Form.
THE WITNESS: I will continue to say that if I were to contrast this with something like nonsteroidal drugs, which can cause the same thing, we have a much

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better grasp of biologic mechanisms whereby nonsteroidal drugs injure the intestines.
I can -- I could. I know you've already told me you don't want to hear me give discourses, but I could tell you multiple mechanisms whereby NSAIDs cause injury, and I don't know those mechanisms here.
BY MR. SLATER:
Q. Move to strike.
I'd just like you to answer my question, please.
A. I do not --
Q. Wouldn't that be a plausible biologic mechanism?
A. And the answer is no.
MR. SLATER: Laura, could you pull out document 30 and mark that as the next exhibit, please.
THE REPORTER: Exhibit 11.
(Document marked for identification purposes as Gutman Exhibit 11.)

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BY MR. SLATER:
Q. Great. Doctor, this is an article titled "Drug-Induced Sprue-Like Intestinal Disease," and I'd like you to turn to page 51, please.
And if you look, there's a section on nonsteroidal anti-inflammatories. You see that?
Do you see that in the bottom right?
A. Oh, yes.
Q. "Further studies are needed to define the precise mechanism involved for the histopathologic mucosal changes following nonsteroidal anti-inflammatory drug use."
Do you see what I just read?
A. I see what you read.
Q. And you don't disagree with that statement, do you?
A. I do disagree with it.
Q. Okay. Do you think the precise mechanism has been identified?
A. I don't think that the choice of mechanism singular is correct. I think there are

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multiple mechanisms.
And not all NSAIDs are going to be the same. However, it's well established that NSAIDs block enzymes that produce prostaglandins, and these prostaglandins are important in things like controlling the mucus production and controlling the bicarbonate secretion in the small intestine and providing cytoprotection to the epithelial layer and, therefore, it's pretty evenly accepted that the depletion of the prostaglandins is a contributing factor to the effect of the NSAIDs.
But there's been other effects that have been also postulated in terms of influx of neutrophils and how that might occur. There's effects on the barrier. All different things like that that have been published.
MR. SLATER: Let me -- let me switch gears now and talk to you about the Basson and Padwal studies and let's -- let's mark both of those. I'm trying to see what number they are.
I think Basson would be number 9, Laura.

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MS. PITTNER: Got it.
MR. SLATER: And Padwal would be 16. Let's make Basson 12 and Padwal 13.
(Document marked for identification purposes as Gutman Exhibit 12.)
(Document marked for identification purposes as Gutman Exhibit 13.)
BY MR. SLATER:
Q. Do you have them both?
A. Yep.
Q. All right. I'm turning to it.
Okay, Doctor. If you look at the Basson article, Table 2.
The total patient years for patients using olmesartan is 860,894; correct?
A. Yes.
Q. And the number of events, which is defined as hospitalization for intestinal malabsorption and celiac disease, is 48; right?
A. Right.
MR. CHRISTIAN: Objection. Objection. Form.

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BY MR. SLATER:
Q. Do you see that?
A. Can you restate that question, please?
Q. Counting the number of events, and events were defined as hospitalization for intestinal malabsorption and celiac disease; right?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: What it says in the abstract for the study design is that the only thing that I'm seeing here is the primary end point was incidence of hospitalization with a discharge diagnosis.
So we don't know if they were necessarily admitted for that problem. That was just a discharge diagnosis was intestinal malabsorption.
BY MR. SLATER:
Q. Okay. Let's -- let me ask the question.
A. And I don't see anything about celiac disease there.

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Q. Well, you don't know where I got celiac disease? It's described in the results section in the first sentence of the discussion of the -- in the article, but I'm happy to limit it the way you want to. So I'll ask the question differently.

For the olmesartan users in Basson, 48 events were listed, which were hospitalizations for intestinal malabsorption; correct?

A. Well, it's hospitalizations where that was the discharge -- discharge diagnosis.

Q. Now, look at Padwal. You can also look at Table 2 in that article.

And you have patients who are hospitalized for any GI disease and the person years there is 17,647; correct?

A. Yes.

Q. Accounted for that; right?

MR. CHRISTIAN: I think we missed the first part, Adam.

BY MR. SLATER:

Q. There were 498 events where people were hospitalized for a GI disease-related

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condition; right?

Isn't that what it says right next to the 17,647?

A. Yes, but I'm not certain whether that's their -- was their primary end point or anything, I think.

Q. I didn't ask you what the primary end point was, did I?

A. No.

Q. I'm just trying to look at the gastrointestinal issues.

So would you also in order to compare the GI issues that were picked up also need to include the next column, the noninfected enteritis and colitis-related admissions?

A. I don't think that you can add them together. I think they're just different criteria.

Q. Okay. As between Basson and Padwal, both relied on an evaluation of administrative claims data; correct?

A. I think that that's true, but one's from France and one's from the US. So that's going to be pretty different.

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Q. In terms of the number of patient years, Basson had a substantially higher number of patient years that were studied; correct? We've just established that?

A. Yes.

Q. The outcome of the Basson study, the data that was generated, when you weigh that, would weigh in favor of a finding of causation; correct?

A. I can't make that conclusion because they had no biopsy data they looked at. It was just hospitalization from discharge diagnosis for malabsorption. So I think that that falls short of making that conclusion.

Q. In your analysis, did you factor in the Basson study?

A. It's on page 7. At the bottom of page 7 of my report.

Q. Yeah, but now we're in your deposition where I'm asking you under oath. So my question is this:

As you sit here now offering your opinions, is the Basson data something that you are considering in forming your opinions?

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MR. CHRISTIAN: Objection. Form.

THE WITNESS: My conclusion about the Basson study is that the data are weak because there's no individual chart review to validate anything. It's just an administrative database. There's no biopsies. There's no other information about the patients.

So I think --

BY MR. SLATER:

Q. Those same comments would apply to the Padwal study as well; right?

MR. CHRISTIAN: Were you finished with your answer?

THE WITNESS: I don't even remember what I was going to say. (Laugh).

In other words, while this might on the surface look like it's higher quality evidence than a case report, it's missing the crucial elements that I just talked to -- talked about, which is that nobody went through all these records of these patients and determined if these

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codings were even correct. So it's just sort of looking --
BY MR. SLATER:
Q. Move --
A. -- looking at a database.
Q. Move to strike.
My question was this.
Well, let me follow up on that first.
So an epidemiologic study as conducted in Basson is not of significance to you because they didn't do a chart review to correlate symptoms and do more of a patient-by-patient analysis.
I understand that correctly?
A. Well, you just said it's not of significance. It's not a binary thing. It's of poor significance. I have factored it into my thinking, but I didn't just throw it out. But I also said that it's of very limited value.
Q. Okay. The same reasons that you say Basson is of limited value, you would -- the same applies to Padwal; right?
A. I mean, I think some of the same

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caveats would ensue for Padwal as well; however, at least it's from the United States. So I might have a better level of confidence about what their administrative data might look like.
Q. Do you have any expertise regarding the level of information and data in the French database they looked at, or are you just biased against French data in favor of US data --
MR. CHRISTIAN: Objection. Form.
BY MR. SLATER:
Q. -- without any basis?
MR. CHRISTIAN: Same objection.
THE WITNESS: I don't have a way to know what the French database looks like.
BY MR. SLATER:
Q. You just like US data better, kind of like people who like California wines better than French wines?
MR. CHRISTIAN: Objection. Form.
THE WITNESS: I've had multiple French people work in my research group. I have two now. So obviously I don't

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have anything against the French.
BY MR. SLATER:
Q. Okay. You have no scientific reason to discount the Basson data just because it's from France, do you?
A. I'm just trying to make the point that I, you know, I would leave it to people that would dissect out this type of data on a daily basis who might be more familiar with the French versus American administrative databases.
Q. Is the answer to my question no, you have no scientific basis to discount the Basson data because it's French?
A. (Laugh). If you put it that way, I suppose I don't. However, it's one was based on discharges for malabsorption and the other is at least more specific in terms of talking about noninfective enteritis and colitis-related admissions. So it seems like --
Q. That's actually the column we didn't talk about it, isn't it, Doctor?
The other column, the one you actually talked about, is gastrointestinal disorders, which is actually broader and less

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specific than malabsorption, isn't it?
A. Again, I don't know what the criteria -- I have to say, I don't know what the criteria for malabsorption were -- was in that administrative database. So that's one. I just don't have much confidence in that.
For example, we talked earlier today about certain laboratory tests that might be indicative of malabsorption, but I don't -- I'm not aware of how they defined it when they coded the patients.
Q. And that's part of your methodology in discounting the data from Basson; correct?
A. I would say so.
Q. I'm going to ask you a couple questions about the ROADMAP study.
You're familiar with that study; correct?
A. Right.
Q. The end points in that study had nothing to do with gastrointestinal conditions; right?
A. I need to just find that again.

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What number is that? Oh, there it is. Okay.

So the original end point of that study was to look at renal complications in diabetics and to see if olmesartan might be beneficial in reducing protein in the urine.

Q. The primary end point in the ROADMAP study was not to evaluate gastrointestinal side effects in any way; correct?

A. That's my understanding.

Q. This population of patients was diabetic; correct?

A. Correct.

Q. Patients who take olmesartan outside of the study population are not all diabetic; correct?

A. Correct.

Q. You did no power calculation to determine whether the ROADMAP study was sufficiently powered to look for sprue-like enteropathy or olmesartan-associated enteropathy; correct?

A. Correct.

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Q. Did you draw any assumption as to whether the study was adequately powered to study that question?

A. No, I didn't.

Q. To study that question, it should not be considered as answering that question; correct?

A. Well, let me explain something. There are these large studies where they have cohorts, like the Framingham Heart Study that -- or the Nurses Study that have proven to be incredibly valuable to go back and reinterrogate.

So, for example, in the Framingham Heart Study, if they were trying to figure out whether aspirin prevented heart attack, one of the benefits of that database is that investigators have gone back and beautifully demonstrated with articles in the New England Journal of Medicine that aspirin turns out to be protective against colon cancer development, but that wasn't how that study was originally designed.

So if you have a lot of patients, you can do -- you can do something useful with

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that data set.

Q. Move to strike.

If the ROADMAP study was not adequately powered to a reasonable degree of medical certainty based on this data, it would not be of any significance in answering the question of causation; correct?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I can't state whether it was adequately powered because that wasn't part of the original design, but you didn't let me before talk about what power is. So I think I'm compelled now to discuss it. So --

BY MR. SLATER:

Q. Doctor, it's not fair for you to give a speech I'm not asking you. You can't just talk about something you want to talk about.

A. Okay. Then I won't answer your question as to whether it was adequately powered.

Q. Okay. I'll ask the question this way.

If the study was not adequately powered just to give an answer -- rephrase.

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If the study was not adequately powered to evaluate severe gastrointestinal side effects in patients taking olmesartan, then it would not be useful in answering the question of causation; right?

MR. CHRISTIAN: Objection. Form.

THE WITNESS: I don't see any -- okay. So in the beginning, they mention the term "severe" in the first sentence, but later they say "We detected no association between treatment and the occurrence of intestinal adverse effects."

So they don't necessarily say that the effects have to be severe. They list a bunch of potential intestinal effects in their table here.

BY MR. SLATER:

Q. Move to strike. Nonresponsive.

If the ROADMAP study was underpowered to evaluate gastrointestinal side effects, it would be unscientific to rely on it to answer the question of causation; correct?

MR. CHRISTIAN: Objection. Form.